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ELECTROCARDIOGRAPHIC CHANGES IN REITER'S SYNDROME*†

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It is generally agreed that induced fever (intravenous vaccine, hyperthermy, inductothermy) provides one of the most effective methods of treatment of Reiter's syndrome (Harkness, 1950; Willcox, 1950), but, although the disease occurs most frequently in young males, the use of this potentially dangerous form of therapy must be conditional on the patient passing a thorough pre-fever investigation. This normally includes complete clinical examination, chest radiography, electrocardiography, and an estimation of the blood urea nitrogen.

During the past year, two young men with Reiter's syndrome have been found on routine examination to exhibit grossly abnormal electrocardiograms without any accompanying clinical evidence of cardiovascular disease. It is impossible to be certain whether or not the relationship is more than adventitious, but, if it should emerge that Reiter's syndrome is capable of producing sub-clinical cardiac damage, this may of itself constitute a contraindication to one of the most effective forms of treatment yet known for the condition.

Master and Jaffe (1934) noted abnormalities of the P-R interval and T waves in nineteen cases of gonococcal arthritis. Gadrat and Morel (1935) found electrocardiographic changes in a man with gonococcal urethritis and arthritis, and Bang (1940) made an electrocardiographic diagnosis of gonococcal myocarditis in six men, five of whom had "recurrent specific arthritis", and the sixth acute urethritis and arthritis.

Lever and Crawford (1944) described the case of a man, aged 37, already in hospital with the complete Reiter's syndrome, who died 2 days after the onset of sub-sternal oppression, cyanosis, and hypotension. An electrocardiogram shortly before death was suggestive of recent anterior myocardial infarction, whereas one taken 6 days previously had been normal.

Candel and Wheelock (1945), in a study of eleven patients with diverse conditions all showing electrocardiographic changes typical of myocarditis, encountered three cases of gonococcal arthritis and myocarditis. Feiring (1946) found prolongation of the auriculo-ventricular conduction time in two cases of Reiter's syndrome. Warthin (1948) noted variations in the T waves in one case consistent with a diagnosis of active myocarditis; treatment with streptomycin produced a "dramatic improvement".

It is well known that a similar syndrome may follow bacillary dysentery. Paronen (1948) described 344 cases during an epidemic of Flexner dysentery: 23 had myocarditis and pericarditis, sixteen myocarditis alone, and three pericarditis alone. The carditis lasted for up to 5½ months and appeared as early as the first week of the disease or as late as the 32nd month.

Lövgren and Masreliez (1949) encountered changes in the electrocardiogram in six out of 22 cases of Reiter's syndrome, and two additional cases with cardiac abnormalities were reported by Trier (1950).

Shapiro, Lipkis, Kahn, and Heid (1949) described electrocardiographic changes in four female cases of acute gonococcal polyarthritis, which "demonstrate a pertinent exception to the axiom that polyarthritis plus an abnormal and unstable electrocardiogram is pathognomonic of acute rheumatic fever". They consider that the electrocardiopathy is apparently caused by a "toxic by-product of the infecting organism" (as suggested by Katz, 1946) rather than a true inflammatory lesion. In two cases the electrocardiogram became normal in 1 month; one case left hospital against advice on the 17th day with a still abnormal electrocardiogram, and the fourth case continued to exhibit an abnormal record on the 39th day after treatment.

Finally, Harkness (1950) found tachycardia (120 to 150 per min.) in two cases of Reiter's syndrome over a period of 5 to 6 weeks during the acute phase.

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Case Histories

Case 1, naval rating, aged 28, married, exposed himself to possible venereal infection on January 22, 1953. Five days later he developed a urethral discharge. A urethral film showed Gram-positive and Gram-negative cocci and pus cells. Treatment was started with procaine penicillin (300,000 units daily), but 4 days later buccal ulceration, pharyngitis, and bilateral conjunctivitis had appeared. He was accordingly admitted to hospital as a probable case of Reiter's syndrome.

Examination.—On February 1 examination showed bilateral conjunctivitis with lacrimation and a mucopurulent conjunctival exudate; shallow white ulcers on the inside of the cheeks, the roof of the mouth, uvula, the anterior fauces, and the posterior pharyngeal wall; small circinate keratotic patches on the glans penis and undersurface of prepuce, but no other skin lesions; no arthritis. A film of the urethral discharge showed numerous pus cells but no organisms, and a mid-stream urine specimen gave no growth on culture. The prostate was slightly enlarged. The erythrocyte sedimentation rate (Westergren) was 10 mm. in the 1st hour, 26 mm. in the 2nd hour. The Wassermann reaction and the Kahn and gonococcal complement-fixation tests were negative.

History.—Gonococcal iritis and arthritis in 1943; urethritis and iritis in 1945; gonorrhoea twice in 1946; iridocyclitis in 1946; urethritis in 1948; Reiter's syndrome (balanitis, urethritis, conjunctivitis) in 1952; and clinical chancroid in 1952.

Therapy.—It was proposed to treat him by fever therapy (intravenous T.A.B. vaccine). The results of the pre-fever investigation on February 3. were as follows:

Blood urea nitrogen: 10 mg. per cent.

Chest *x* ray: Normal.

Electrocardiogram: Normal sinus rhythm. Rate 65 per min. P-R interval 0·16 sec. The record was highly abnormal, showing slight ST elevation and upright T waves in three standard leads; ST depression and inverted T waves in aVR; ST elevation and low upright T waves in aVF; ST elevation in all chest leads, most marked in V3; in V4 a 3 mm. Q wave preceding a tall R wave; in V5 Q wave measured only 2 mm. The changes recorded were those of sub-epicardial or pericardial damage, with the most marked changes over the anterior surface of the heart. The wide distribution of the ST/T changes suggested pericarditis. The decreasing amplitude of the Q wave from V4 to V5 suggested localized sub-epicardial damage.

Repetition of the electrocardiogram on February 10, 17, 24, and on March 5, 1953, showed no significant change in the above findings.

Fever therapy was therefore not employed, treatment being by local instillations into the eye (albucid 30 per cent., atropine 1 per cent., cortisone) and anterior urethral irrigations. In addition he received a course of 11·5 mega units crystalline penicillin G for furunculosis of the neck due to *Staphylococcus aureus*. After 1 month in hospital he developed marked keratoderma blennorrhagica of the soles of the feet and the erythrocyte sedimentation rate was still elevated (9 mm. in the 1st hour, 20 mm. in the 2nd hour). He was then transferred to a convalescent unit where he made a symptomatic recovery.

Later Developments.—A year later, on January 17, 1954, he again risked extra-marital coitus and 8 days later exhibited dysuria, frequency, a urethral discharge, bilateral conjunctivitis, and injection of the buccal and pharyngeal mucosa with superficial ulceration. The stained film of the urethral discharge revealed large numbers of pus cells and a few Gram-negative extracellular diplococci (morphologically resembling gonococci). The Wassermann reaction and the Kahn and gonococcal complement-fixation tests were negative. The erythrocyte sedimentation rate was 6 mm. in the 1st hour, 20 mm. in the 2nd hour. Culture of mid-

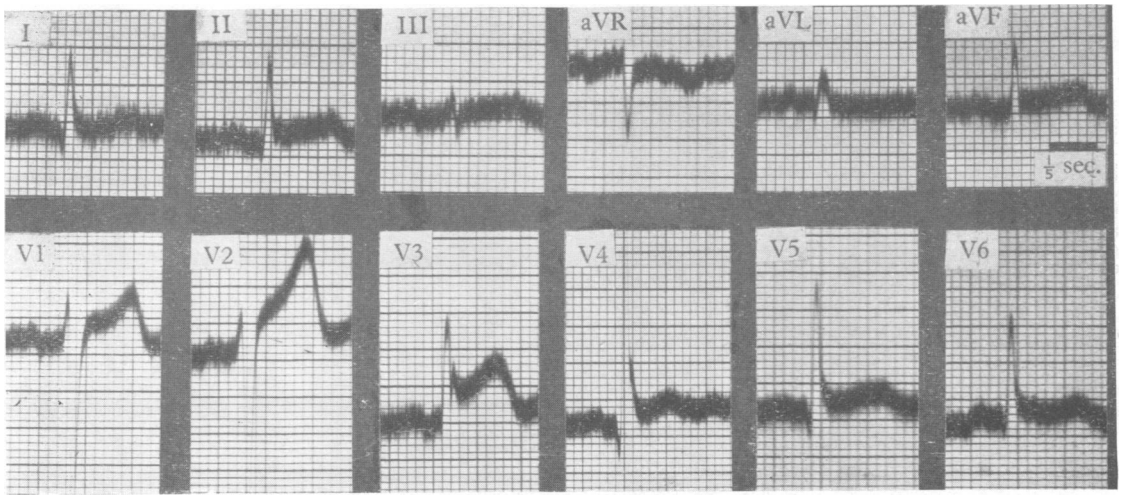

FIG. 1.—Case 1, illustrating changes suggestive of pericardial and sub-epicardial damage. (Widespread ST elevation; decrease in amplitude of Q wave from V4 to V5.

stream urine gave a growth of Gram-negative diplococci overgrown by diphtheroids. A stained film of the conjunctival exudate showed pus cells but no organisms. The blood urea nitrogen was 19 mg. per cent.

On January 27 the electrocardiogram was reported on thus :

Comparison with the record taken on March 5, 1953, shows little change except that the T wave in V4 is now very shallow and inverted, and that the T waves in V5 and V6 are flat. The ST shifts certainly suggest the presence of pericarditis and are very unusual.

Again fever therapy was regarded as contraindicated and treatment consisted of saline eye baths, glycerine of thymol mouthwashes, crystalline penicillin G (200,000 units 4-hrly to a total of 6 mega units), and two courses of terramycin (20 g. and 15 g. respectively). Symptomatic recovery followed the second course of terramycin, but repetition of the electrocardiogram on February 11, March 8, and April 9, 1954, showed persistence of the abnormalities noted above.

Case 2, physical-training instructor, aged 30, married, developed mild balanoposthitis on December 12, 1953. There had been extra-marital coitus 2 weeks previously. He had no previous history of venereal disease. Two days later a urethral discharge appeared and the left knee became painful and swollen. A stained film of the discharge showed pus cells +++, Gram-negative diplococci morphologically resembling gonococci+. Culture gave a growth of similar organisms but biochemical confirmation was not obtained. The Wassermann reaction and the Kahn and gonococcal complement-fixation tests were negative. A single injection of 600,000 units oily procaine penicillin was given.

A week later there was no discharge and no pyuria, and a midstream urine culture was sterile. The left knee was still painful, however, and the erythrocyte sedimentation rate was 13 mm. in the 1st hour, 23 mm. in the 2nd hour. On December 29 he was admitted for pre-fever investigation, which gave the following results :

Clinical examination of cardiovascular system : NAD.
Blood pressure : 124/80 mm. Hg.
Blood urea nitrogen : 14 mg. per cent.
Chest *x* ray : Normal.
Electrocardiogram : Normal sinus rhythm. Rate 71 per min. P-R interval 0·2 sec. Horizontal heart. The record showed the presence of anterior myocardial infarction with involvement of the septum.

Accordingly fever therapy was regarded as contraindicated and treatment was restricted to local measures (radiant heat, kaolin poultices). *X*-ray examination of the left knee showed soft tissue swelling, with localized sub-articular osteoporosis most marked in the peripheral areas. The other joints were unaffected, but about this time slight angular conjunctivitis was noted in the right eye. The prostate was normal on palpation and the prostatic fluid contained neither pus cells nor organisms.

On December 12 repetition of the electrocardiogram confirmed the previous findings. The erythrocyte sedimentation rate was 6 mm. in the 1st hour, 11 mm. in the 2nd hour. Plasma fibrinogen was 0·8 g. per cent. A 24-hr specimen of urine tested for urobilinogen revealed a slight trace (" not estimable ").

One month later the patient was discharged from hospital. An electrocardiogram at this time was identical with the previous ones.

Three months later an electrocardiogram was reported as follows :

Comparison with the previous record shows steeper inversion of T in V3. T is flat in V5 and V6.

After leaving hospital he felt perfectly well and resumed his previous occupation.

Summary and Conclusions

Two cases of gonorrhoea complicated by Reiter's syndrome in young men are described. In both cases the electrocardiogram was highly abnormal yet neither exhibited any clinical cardiovascular abnormality. It is uncertain whether the relationship is significant or merely adventitous, but the ages

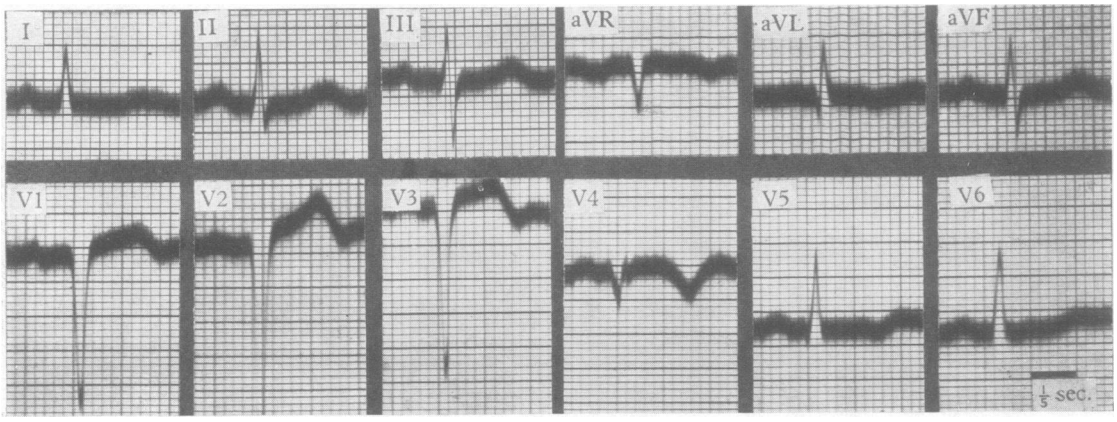

FIG. 2.—Case 2, illustrating changes suggestive of anterior myocardial infarction. (ST elevation and inversion of T waves in chest leads.)

of the patients and the persistence of the electrocardiogram changes are quite unlike those found in coronary arterial disease.

It is suggested that the changes in the electrocardiogram which have frequently in the past been ascribed to toxic gonococcal carditis are possibly a further manifestation of Reiter's syndrome, which may occur alone or as a complication of gonorrhoea. It is further suggested that electrocardiography should form part of the routine investigation of all cases of Reiter's syndrome, whether or not fever therapy is contemplated, in an attempt to elucidate the problem.

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REFERENCES

Bang, O. (1940). *Brit. med. J.*, **1**, 117.
Candel, S., and Wheelock, M. C. (1945). *Ann. Intern. Med.*, **23**, 309.
Feiring, W. (1946). *Ibid.*, **25**, 498.
Gadrat, J., and Morel, L. (1935). *Bull. Soc. franç. Derm. Syph.*, **42**, 1849.
Harkness, A. H. (1950). "Non-Gonococcal Urethritis." Livingstone, Edinburgh.
Katz, L. N. (1946). "Electrocardiography", 2nd ed., p. 230. Lea and Febiger, Philadelphia.
Lever, W. F., and Crawford, G. M. (1944). *Arch. Derm. Syph.* (Chicago), **49**, 389.
Lövgren, O., and Masreliez, N. (1949). *Nord Med.*, **42**, 1299.
Master, A. M., and Jaffe, H. (1934). *Proc. Soc. exp. Biol.* (*N.Y.*), **31**, 931.
Paronen, I. (1948). *Acta med. scand.*, Suppl. 212.
Shapiro, E., Lipkis, M. L., Kahn, J., and Heid, J. B. (1949). *Amer. J. med. Sci.*, **217**, 300.
Trier, M. (1950) *Acta med. scand.*, **138**, Suppl. 239, p. 123.
Warthin, T. A. (1948). *Amer. J. Med.*, **4**, 827.
Willcox, R. R. (1950). "A Text-book of Venereal Diseases." Heinemann, London.